PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/001551	08.04.2004	10.04.2003

International Patent Classification (IPC) or both national classification and IPC
G01N21/17, G01N25/48, G01N33/487, G01N33/53

Applicant
PIEZOPTIC LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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JC05 Rec'd PCT/PTO 07 OCT 2005

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/001551
10/552702

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/001551

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	7,8,17,18,22-26,29
	No:	Claims	1-6,9,11-16,19-21,27,28
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-29
Industrial applicability (IA)	Yes:	Claims	1-29
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: WRIGHT J D ET AL: 'Development of a piezo-optical chemical monitoring system' SENSORS AND ACTUATORS B, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 51, no. 1-3, 31 August 1998 (1998-08-31), pages 121-130, XP004153998 ISSN: 0925-4005

D2: GIBSON C A ET AL: 'Kinetic factors in the response of piezo-optical chemical monitoring devices' SENSORS AND ACTUATORS B, ELSEVIER SEQUOIA S.A., LAUSANNE, CH, vol. 51, no. 1-3, 31 August 1998 (1998-08-31), pages 238-243, XP004154016 ISSN: 0925-4005

D3: FR-A-2 715 226 (UNIV REIMS CHAMPAGNE ARDENNE)

D4: WO 90/13017 A (HEALTH LAB SERVICE BOARD) cited in the application

2. **Novelty (Art. 33(2) PCT) and Inventive Step (Art. 33(3) PCT):**

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of **claims 1-6, 9, 11-16, 19-21, 27, 28** is not new in the sense of Article 33(2) PCT, and because the subject-matter of **claims 7, 8, 17, 18, 22-26, 29** does not involve an inventive step in the sense of Article 33(3) PCT.

2.1 **Apparatus claim 1:**

2.1a **D1 and D2** disclose (the references in parentheses applying to these documents):
-- A device *for* detecting energy (heat) generated by non-radiative decay in a substance (reagent spots) on irradiation with electromagnetic radiation (**D1**: title; abstract; fig. 2)(**D2**: title, abstract; fig. 1);
-- a radiation source (LED) *adapted to* generate a series of pulses of electromagnetic radiation (**D1**: fig. 2; page 121, right column, lines 16-17, "chopped light"; page 124, left column, lines 1-3)(**D2**: fig. 1; page 238, left column, lines 20-21, "chopped light");

-- a transducer having a pyroelectric *or* piezoelectric element and electrodes *which is capable of* transducing the energy (heat) generated by the substance into an electrical signal (**D1**: fig. 2, "PVDF film"; abstract; page 121, right column, lines 1-7)(**D2**: fig. 1, "PVDF film"; abstract; page 238, left column, line 18, right column, lines 1-3);
-- a detector *which is capable of* detecting the electric signal generated by the transducer (**D1**: implicitly disclosed on page 121, right column, lines 7-10)(**D2**: implicitly disclosed on page 238, right column, lines 3-5);
-- the detector is *adapted to* determine the time delay between each pulse of electromagnetic radiation from the radiation source and the generation of the electric signal (**D1**: page 122, left column, lines 14-16; page 124, left column, lines 1-9, "variable phase lag")(**D2**: title, "kinetic factors"; fig. 3 shows detected signals as the distance of the heat source from the transducer is varied; fig. 4 shows the "phase lags").

It should be noted that D2 is directly referred to in D1 (see page 124, left column, par. 5, "Phase lag... Details of this behaviour are given elsewhere [4]". For the discussion on patentability, both documents can therefore also be seen as one document, whereby the information disclosed in D2 is implicitly disclosed in D1.

2.1b It should be noted, that **D3** also discloses (the references in parentheses applying to this document):
-- A device *for* detecting energy generated by non-radiative decay in a substance on irradiation with electromagnetic radiation (fig. 1, 2; page 4, lines 5-34; page 5, line 23 - page 6, line 16);
-- a radiation source 1 *adapted to* generate a series of pulses 3 of electromagnetic radiation F (page 5, lines 24-31; page 4, lines 10-16);
-- a transducer 4 having a pyroelectric *or* piezoelectric element and electrodes *which is capable of* transducing the energy generated by the substance into an electrical signal (page 6, lines 3-7; page 4, lines 17-19);
-- a detector 5, 6, 7 *which is capable of* detecting the electric signal generated by the transducer (page 6, lines 7-13; page 4, lines 20-22);
-- the detector 7 is *adapted to* determine the time delay between each pulse of electromagnetic radiation from the radiation source and the generation of the electric signal (page 6, lines 13-14; page 4, lines 23-27; page 8, lines 11-14, 24-

25; fig. 7).

2.1c It should be noted, that **D4**, cited in the application, also discloses (the references in parentheses applying to this document):
-- A device *for* detecting energy generated by non-radiative decay in a substance on irradiation with electromagnetic radiation (fig. 1);
-- a radiation source 24 *adapted to* generate a series of pulses of electromagnetic radiation (page 5, lines 22-27);
-- a transducer 10 having a pyroelectric *or* piezoelectric element and electrodes 12, 14 *which is capable of* transducing the energy generated by the substance into an electrical signal (page 5, lines 10-11, 32-37);
-- a detector *which is capable of* detecting the electric signal generated by the transducer (implicitly disclosed in page 5, line 36 - page 6, line 5, "microcomputer");
-- the detector is *adapted to* determine the time delay between each pulse of electromagnetic radiation from the radiation source and the generation of the electric signal (implicitly disclosed in page 4, lines 17-19: "the depth... that is probed"; page 5, lines 25-28; page 6, lines 1-3, "reference signal" of light modulation via "line 28" to "phase-locked" detector).

2.2 The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding **independent method claim 19**, which therefore is also considered not new.

2.3 What has been said above, at least with respect to D1, D2 and D4, with reference to apparatus claims 1 concerns **independent method claims 20 and 28** mutatis mutandis.

2.4 **Dependent claims 2-18, 21-27, and 29** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, see documents **D1-D4** and the corresponding passages cited in the search report:

- **Claims 2, 14**: at least one reagent proximal to the transducer, the reagent having a binding site which is *capable of* binding an analyte; reagent is adsorbed on to

the transducer (**D1**: page 121, right column, line 5)(**D2**: fig. 1; page 243, right column, lines 5-8)(**D4**: fig. 1, reagent 16);
- **Claim 3, 21**: reagent is antibody (**D4**: page 6, line 15)(**obvious** with respect to **D2**, fig. 1; page 243, right column, lines 5-8);
- **Claims 4, 5, 6, 15**: no clearly claimed apparatus features; the substance/analyte does not form part of the claimed device;
- **Claims 7, 8**, 18: reagent is a first nucleic acid; the reagent contains avidin or derivatives thereof (**obvious** with respect to **D2**, fig. 1, page 243, right column, lines 5-8; and **D4**: page 6, lines 8-17);
- **Claim 9**: the device is *suitable for* monitoring the progress of a reaction between reactants; at least one substance proximal to the transducer, the substance being *capable of* absorbing the electromagnetic radiation generated by the radiation source to generate energy (**D2**: page 238, right column, lines 10-11, 19-20, 23-24)(**D3**, page 13, lines 30-32; page 14, lines 8-1118-22);
- **Claim 10, 29**: the reaction is a polymerisation or depolymerisation reaction (**obvious** with respect to **D2**, fig. 1, page 243, right column, lines 5-8; and **D4**: page 6, lines 8-17);
- **Claims 11, 12**: time delay is at least 5 ms; no greater than 500 ms (**D2**: fig. 4);
- **Claim 13**: light (**D1**: page 121, right column, line 17)(**D2**: page 238, left column, line 21)(**D3**: page 5, line 25)(**D4**: page 5, lines 22-23);
- **Claim 16**: well for holding the liquid in contact in contact with the transducer (**D1**: page 122, right column, lines 21-23: pores)(**D3**: fig. 5);
- **Claim 17**: chamber for storing additional reagents (**non-inventive** design option);
- **Claim 18**: additional reagent is a labelled antibody;
- **Claims 22-26**: complex with labelled antibody, antigen, ... (**obvious** with respect to **D2**, fig. 1, page 243, right column, lines 5-8; and **D4**: page 6, lines 8-17);
- **Claim 27**: see D1-D4.

2.5 **Comment/summary**:

The device of the invention is known from **D1-D4**. The new, but non-inventive, feature is the application of said known device for analysing other samples, such as avidin/biotin.

3. Industrial applicability (Article 33(4) PCT):

The requirement of Art. 33(4) PCT as to industrial applicability is fulfilled for all claims.

Re Item VII
Certain defects in the international application (form or content)

4.1 Contrary to the requirements of Rule 5.1(a)(ii) PCT, **the relevant background art** disclosed in the **documents D1, D2, and D3** is not mentioned in the description, nor are these documents identified therein.

4.2 The features of the claims are not provided with **reference signs** placed in parentheses (Rule 6.2(b) PCT).

4.3 According to the requirements of Rule 11.13(l) reference signs not appearing in the description shall not appear in the drawings, and vice versa. This requirement is not met in view of the **reference sign "13"**, page 7, third paragraph (not in fig. 2).

Re Item VIII
Certain observations on the international application (clarity)

5.1 The dependency of **Claim 9** is not clear (Art. 6 PCT). The claim does not define all features of independent claim 1 and is therefore incorrectly formulated as being dependent on the latter. Claim 1 does not define "A device for monitoring the progress of a reaction between reactants".

5.2 Although **Method claims 19, 20, and 28** have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore **lack conciseness**.

Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.
Hence said claims do not meet the requirements of Article 6 PCT.

It appears to be possible to define the relevant subject-matter in terms of a minimum number of independent claims in each category followed by dependent claims covering features which are merely optional (Rule 6.4 PCT).

5.3 The dependency of **claims 14, 15 and 17** is not clear (Art. 6 PCT), since the reagent is for the first time defined in claim 2.

5.4 Some of the features (lines 16-17, 22-26) in the apparatus claim 2 relate to a method of using the apparatus rather than clearly defining the apparatus in terms of its technical features. The intended limitations are therefore not clear from this claim, contrary to the requirements of Article 6 PCT.

5.5 **Claims 4, 5, 6, 15** do define additional apparatus features; the substance/analyte does not form part of the claimed device defined in claim 1.

5.6 The **term "energy"** used in **claims 1, 9, 19, 20, 28** is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT). However, it is clear from the description (see the **"key feature"** on page 3, line 32-33), that **heat is generated**.